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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/804,733	03/13/2001	Qi Wang	MTC 6614.1	2031

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EXAMINER

LEFFERS JR, GERALD G

ART UNIT PAPER NUMBER

1636

DATE MAILED: 05/04/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

# Office Action Summary

Application No.

09/804,733

Applicant(s)

WANG ET AL.

Examiner

Gerald G. Leffers Jr., PhD

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

## Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

## Status

- 1) ☒ Responsive to communication(s) filed on 15 February 2005.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

## Disposition of Claims

- 4) ☒ Claim(s) 1-20 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1-20 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

## Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 13 March 2001 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

## Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

## Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)  
Paper No(s)/Mail Date 6/14/01; 11/17/02; 3/22/04

- 4) ☐ Interview Summary (PTO-413)  
Paper No(s)/Mail Date. \_\_\_\_\_
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: \_\_\_\_\_

**DETAILED ACTION**

***Response to Amendment***

Receipt is acknowledged of an amendment and response, filed on 2/15/2005, in which the nonelected claims were cancelled (i.e. claims 21-118) and in which several claims were amended (claims 1, 12 & 15). Claims 1-20 are pending and under consideration in the instant application.

Any rejection of record in the instant application not addressed herein is withdrawn. This action is not final as there are new grounds of rejection presented herein that were not necessitated by applicants' amendment of the claims in the response filed 2/15/2005.

***Information Disclosure Statements (IDS's)***

Receipt is acknowledged of an IDS filed on 3/22/2004. The signed and initialed PTO Form 1449 has been mailed along with this action.

In the previous office action, the examiner indicated that the nonpatent literature documents cited in the IDS's filed on 6/14/01 & 1/17/02 were not located with the file and that the nonpatent literature documents had not been considered. The patent and patent application documents cited on these earlier IDS's were considered, however, and the corresponding PTO 1449's mailed along with the previous office action on 11/19/2003. Applicants subsequently demonstrated in the papers filed on 3/22/2004 that the cited references from the 6/14/01 & 1/17/02 IDS's were provided to the Office. The examiner has since obtained the nonpatent literature references cited on the IDS's filed on 6/14/01 & 1/17/02. Accordingly, the same patents and patent applications cited on the copies of the 6/14/01 & 2/17/02 PTO 1449's mailed with this action have been lined through so as to prevent duplicate citation of the same patents

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and/or applications on any patent to issue from the instant application. All references cited on the 6/14/01, 1/17/02 & 3/22/2004 IDS's have now been considered.

***Claim Rejections - 35 USC § 112***

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter that the applicant regards as his invention.

Claims 1-20 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. **These are new rejections.**

Claim 1(a) is vague and indefinite in that the metes and bounds of the phrase "...providing a first pool of polynucleotides, said pool of polynucleotides comprising at least two tandem repeats of sequences encoding a portion of said recombinant protein, wherein said tandem repeats contain degenerate nucleotide sequences encoding for said recombinant protein in accordance with the degeneracy of the genetic code..." are unclear. First, it is unclear as written whether the tandem repeats of nucleic acid comprising degenerate nucleotide sequences *necessarily* encode the *entire* recombinant protein (e.g. the polynucleotide described in Working Example 1 of the instant specification that encodes a protein consisting of a tetramer of the sequence LKPMN) or can encode only a portion of the recombinant protein. Secondly, it is unclear with regard to what reference sequence the tandem repeat sequences comprise degenerate codons in accordance with the genetic code. For example, one could interpret the claim to specify that the tandem repeat sequences are degenerate with regard to a sequence that is not specified in the claims (e.g. alternative codon usage relative to an allelic sequence obtained

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from a species having different codon usage). Alternatively, the claim can be interpreted to mean that the tandem repeats are degenerate *with regard to one another* (i.e. the tandem repeats encode the same amino acid sequence but use different codons to do so). Upon reading the specification, it appears that (i) the invention encompasses methods where the tandem repeats encode only a portion of the recombinant protein produced by the nucleotide chain extension method, and (ii) the tandem repeats contain degenerate nucleotide sequences with regard to one another.

Claim 3 is vague and indefinite in that there is no clear and positive prior antecedent basis for the term “said tandem repeats” in claim 1, upon which claim 3 is dependent. For example, claim 1 recites the term “tandem repeats” only in the context of nucleic acid sequences whereas the rejected claim refers to the “tandem repeats” in the context of a protein sequence. It would be remedial to amend claim 1 or claim 3 to clearly provide antecedent basis for the use of the term “said tandem repeats” with reference to the amino acid sequence of the recombinant protein. Claims 10 & 17 also recite the term “tandem repeats” in terms of the protein sequence without any clear antecedent basis for doing so.

Claims 5-8 are vague and indefinite in that the metes and bounds of the phrase “...encode polypeptides comprising at least 25% [50%, 75% or 90%] of a desired amino acid...” are unclear. As currently written, it is unclear what amount of amino acid residues of the desired amino acid would satisfy the claim limitation. As written, the claims appear to specify a particular mass or concentration of a particular amino acid without any reference for the recited percentage (e.g. 1 nmole, 10 nmoles, etc.). It appears from reading the instant specification, however, that the cited phrase is intended to specify that the recited percentage of a desired

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amino acid is relative to the amino acid content of the recombinant protein. Thus, the phrase “at least 25% of a desired amino acid” may be interpreted as meaning that desired amino acid makes of 25% of the amino acid content of the recombinant protein. If this interpretation is correct, it would be remedial to amend the claim language to more clearly indicate what is intended by the cited phrase.

Claim 13 is vague and indefinite in that there is no clear and positive prior antecedent basis for the term “said vector” in claim 10, upon which claim 13 is dependent. There are at least two vectors present in the method recited in claim 10, making it unclear which is referred to by the cited term.

Claim 17 is vague and indefinite in that there is no clear and positive prior antecedent basis for the phrase “...wherein said expression cassette further comprises an additional nucleotide sequence encoding an enzyme capable of cleaving said recombinant protein between said tandem repeats.” Claim 10, upon which claim 17 is dependent, already recites the presence of a nucleotide sequence encoding an enzyme capable of cleaving the recombinant protein, making it unclear if there are necessarily at least two such encoding sequences required for the method of claim 17.

#### *Examiner's Note*

The teachings of Kiyotaka Shiba (European Patent Application EP 0812911 A2; published 12/17/1997) appear to be the closest prior art of record. Shiba teaches methods for forming a macromolecular microgene polymer that results in a polynucleotide coding sequence that comprises several repeat sequences of the same gene (e.g. Figure 1(a)-1(c); Example 1).

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Shiba does not anticipate the instant invention in that it does not teach step 1(a) of the instant claims. The instant specification defines the term “tandem repeats” in the specification as follows (examiner’s emphasis added):

“As use[d] herein, the term “tandem repeat(s)” means either multiple copies of a nucleotide sequence which encodes the same amino acid sequence within a single polynucleotide or repeating amino acid sequences within a single peptide or protein.” (page 9, lines 2-4 of the instant specification).

Even in Examples 6 & 7, where a pool of oligonucleotides is provided that comprises variable positions within one of the first oligonucleotides used for nucleotide chain extension (e.g. see Figure 9 where KY-812 varies at positions n=3 & n=11 by comprising C, G, T or A at these positions), Shiba does not teach or suggest providing a first pool of polynucleotides comprising at least two tandem repeats of sequences as explicitly defined in the specification (e.g. see page 9, lines 2-4; Figures 1(a)-1(b) of the instant specification). That is, neither of the pools of polynucleotides used in the initial chain extension reactions taught by Shiba comprise, as part of the same polynucleotide, repeated nucleic acid sequences that encode the same amino acid sequence. Therefore, the teachings of the Shiba application do not anticipate the pending claims.

### ***Conclusion***

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Gerald G. Leffers Jr., PhD whose telephone number is (571) 272-0772. The examiner can normally be reached on 6:30-4:00.

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If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Remy Yucel can be reached on (571) 272-0781. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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Gerald G Leffers Jr., PhD

Primary Examiner

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*Gerald G Leffers Jr.*  
**GERRY LEFFERS**  
**PRIMARY EXAMINER**